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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/735,335

12/12/2003

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EXAMINER

MAIER, LEIGH C

ART UNIT

PAPER NUMBER

1623

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/735,335	Applicant(s) MADHAVI ET AL.	
	Examiner Leigh C. Maier	Art Unit 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 November 2007 and 03 July 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,5-7,11,15-17 and 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,5-7,11,15-17 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1, 5-7, 11, 15-17 and 19 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Applicant states “[e]ach of the cited references has been discussed in detail in a prior response and such remarks are expressly incorporated herein by reference.” The examiner will address the remarks/arguments submitted in the response filed July 3, 2006.

### ***Claim Rejections - 35 USC § 102***

Claims 1, 5-7, 11, 15-17 and 19 are again rejected under 35 U.S.C. 102(b) as being anticipated by Mele et al (Carbohydr. Res., 2002), as set forth in the previous Office action.

Mele teaches the preparation of a complexes comprising lycopene with  $\alpha$ -cyclodextrin or  $\beta$ -cyclodextrin. The complexes are isolated by freeze-drying. See 1<sup>st</sup> paragraph under section 3 at page 1134. The reference is silent regarding the molar ratio of the complex that is formed. However, given the structure of carotenoids and how cyclodextrins form complexes in general, it would be expected that the cyclodextrin:carotenoid ratio would be about 1:1 or 2:1. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

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Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant argues that it is not obvious from the reference that freeze-drying is the preferred method for drying a carotenoid-cyclodextrin complex. The fact that reference does not address the relative desirability of the drying method is not relevant because a freeze-dried product is, in fact, disclosed.

Applicant further contends that there is no experimental evidence on the bioavailability of the reference complex. Again, a product, meeting the physical limitations of the claims is disclosed. The burden is on Applicant to demonstrate that the disclosed product does not comprise the recited functional limitations regarding bioavailability.

Claims 1, 5, 11, 15 and 19 are again rejected under 35 U.S.C. 102(b) as being anticipated by Mele et al (Carbohydr. Res., 1998), as set forth above.

Mele teaches the preparation of a complex of  $\beta$ -carotene and  $\gamma$ -cyclodextrin that is isolated by freeze-drying. See 1<sup>st</sup> paragraph under section 2 at page 262. The reference is silent regarding the molar ratio of the complex that is formed. As discussed above, it would be expected that the cyclodextrin:carotenoid ratio would be about 1:1 or 2:1, and the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art.

Applicant's arguments regarding Mele are addressed above.

Claims 1, 6 and 7 are again rejected under 35 U.S.C. 102(b) as being anticipated by Pfitzner et al (BBA, 2000) as set forth in the previous Office action.

Pfitzner teaches the preparation of M $\beta$ CD complexes with  $\beta$ -carotene, lycopene, lutein and zeaxanthin. See section 2.2. The products are not isolated by freeze-drying. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) As above, the burden is on Applicant to demonstrate a novel or nonobvious difference.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant objects to this reference because of the variations in stability and complexation ability of carotenoids with various cyclodextrins, and the authors are unable to account for the results seen. While scientifically interesting, this is not germane to the fact that the reference does, in fact, appear to disclose a product that meets the limitations of the claims.

Applicant further argues that the complexation improves the bioavailability of the carotenoid. As discussed above, if the product in the product-by-process claim is the same as or obvious from a product of the prior art, the burden is on Applicant to demonstrate a novel or nonobvious difference.

***Claim Rejections - 35 USC § 103***

Claims 1, 5-7, 11 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mele et al (Carbohydr. Res., 2002).

Mele teaches as set forth above. The reference discusses the desirability of increasing the bioavailability of carotenoids, including lycopene,  $\beta$ -carotene, lutein and zeaxanthin, for their use in products such as drugs and cosmetics. One method for doing this is the encapsulation of the carotenoid in a cyclodextrin. See section 1. The reference does not exemplify complexes of all the carotenoids with a cyclodextrin.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare cyclodextrin ( $\alpha$  or  $\beta$ ) complexes with any of the carotenoids discussed by Mele in order to improve their bioavailability as taught in the reference. One of ordinary skill would be motivated to isolate them by freeze-drying because that is the method taught in the reference. In the absence of unexpected results, one of ordinary skill would reasonably expect success in preparing these compounds by this method because it is expressly suggested in the art.

Applicant's arguments with respect to Mele are addressed above.

Claims 1, 5-7, 11 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mele et al (Carbohydr. Res., 2002) in view of either of (1) Mele et al (Carbohydr. Res., 1998) or (2) Szente et al (J. Incl. Phenom., 1998).

Mele '02 teaches as set forth above. The reference does not teach the full range of recited cyclodextrins.

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Mele '98 and Szente teach as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare complexes comprising any of the carotenoids discussed by Mele '02 with any cyclodextrin known to complex with a carotenoid, such as those taught by Mele '98 or Szente. One of ordinary skill in the art would be motivated to prepare these complexes in order to increase their bioavailability as taught by Mele '02. The artisan would reasonably expect success in isolating them by freeze drying because this method is also taught by this reference.

Applicant has submitted data purporting to be evidence of unexpected results. Any such evidence would not overcome rejections to subject matter specifically rejected as being anticipated, discussed above. Although it is the opinion of the examiner that the full scope embraced by the claims is anticipated or obvious, it is noted that every possible carotenoid/cyclodextrin combination is not anticipated, and there may be unexpected results with one or more of these combinations.

The data submitted by Applicant compares the bioavailability spray-dried lutein/ $\gamma$ -CD with freeze-dried lutein/ $\gamma$ -CD and demonstrates that freeze-dried complex has greater bioavailability in an *in vitro* assay. The examiner is not persuaded that this comparison is conclusive in the context of the invention. The *in vitro* assay demonstrates that the freeze-dried product has greater uptake by the Caco-2 cells. However, intestinal absorption is only one factor determining bioavailability. Another factor is degradation or metabolism that occurs before absorption. Applicant admits "the carotenoids are not completely protected from degradation by the complexation, [so] further formulations are necessary for incorporation into the soft gelatin capsules" and further discusses the need for other excipients. See page 7, lines 22-30. It may be

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that without other excipient(s) the carotenoid is so degraded before it gets to the point of being absorbed, that the added uptake by the freeze-dried product is negligible. Furthermore, it may be that one would see a different result in the in vitro assay if another protective excipient, such as oil, were present. This cannot be determined by the data submitted.

Applicant's remarks of July 3, 2006 do not address this particular combination of references as set forth in the previous Office action. A discussion of each reference individually does not constitute a persuasive argument based on a combination of references. The rejection is maintained for reasons set forth previously.

It is further noted that, as Applicant points out, Pfitzner teaches the variability in interactions between carotenoids and various cyclodextrins. Therefore, the examiner expects that Applicant would agree that even if the proffered data—limited to lutein and  $\gamma$ -cyclodextrin—were evidence of unexpected results, they would not be nearly commensurate with the scope of the claims.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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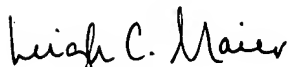
however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Examiner's hours, phone & fax numbers***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday and Friday 9:00 to 5:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

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Leigh C. Maier  
Primary Examiner  
January 3, 2008